Remarks

Upon entry of the foregoing amendment, claims 1, 4, 5, 7, 8, 11, 13-16, 18 and 26-28 are pending in this application. Claims 2, 3, 6, 9, 10, 12, 17, 19 and 20 have been cancelled. Claim 1 is the sole pending independent claim under examination. Claims 1, 4, 5, 7, 8, 11, 13-16, 18 and 26-28 are under examination. It is noted that original claims 22-24 have been rewritten as new claims 26-28 and now depend from claim 1.

Claim 1 has been rewritten to more clearly claim the invention. Support for the amendments to claim 1 is found, for example, in original claim 1; page 12, line 24; and, elsewhere throughout the specification.

Support for the amendments to claims 1, 4, 5, 7, 8, 11, 13-16, 18 and 26-28 for changing "immunization system" to "method" is found, for example, in original claim 21; and, elsewhere throughout the specification. See, *e.g.*, page 5, lines 13-17.

Support for the amendments to claims 4, 7 and 8, for "chemical" indicator is found in original claim 1; and, elsewhere throughout the specification. The amendment was made to provide antecedent basis for "indicator."

Support for the amendments to claim 11, changing the dependency from claim 10 to claim 1, is found in original claim 1, and was made to provide correct claim dependency in view of the cancellation of claim 10.

Support for the amendment to claim 16, removing the word "immunization," is found in amended claim 1. Claim 16 was amended to provide correct antecedent basis.

Claim 13 was amended to delete "paint" and "powders" as recommended by the Examiner.

Claims 15 and 18 were amended to provide for correct claim dependency.

Support for new claims 26-28 is found in original claims 22-24 and elsewhere throughout the specification.

It is believed that no new matter has been introduced by this amendment.

Inventorship

Applicants thank the Office for accepting the request to correct the inventorship, filed May 21, 2002.

Declaration under 37 CFR § 1.63

Applicants acknowledge the declaration filed under 37 CFR § 1.63 has been considered.

Declaration under 37 CFR § 1.132

Submitted herewith is an unexecuted declaration by Dr. G. Glenn. Applicants will submit an executed declaration shortly. Dr. Glenn was unavailable at the time the reply was filed. The Examiner is requested to consider the unexecuted declaration for the teachings therein until the executed declaration is matched with the file.

Prior Rejections

Rejection of claims 1-4, 10, 12, 13 and 20 under 35 U.S.C. § 102(a)

The Office has maintained the rejection of claims 1-4, 10, 12, 13 and 20 under 35 U.S.C. § 102(a) as being anticipated by Glenn *et al.* (Infection and Immunity 67(3): 1100-1106, March 1999; PTO 892) [Glenn]. The rejection is respectfully traversed. Claims 2, 3, 10, 12 and 20 have been cancelled.

The Office alleges the document anticipates the claimed invention. In maintaining the rejection the Office takes note of the lineage of the instant application and traces the priority date back to November 14, 1996. The Office paid particular attention to the language of claim 1 ("Further, the recitation of 'a marking formulation, said marking formulation comprising at least one

chemical indicator, the presence of said indicator serving to provide a readily discernible indication of the use of said immunization formulation' in base claim has no support in USSN 08/896,085, filed July 1997, now USPN 5,980,898 which in turn is a continuation-in-part of Serial No. 08/749,164, filed November 14, 1996, now USPN 5,910,306") in assessing the priority date and denied the instant application benefit of the July 1997 and November 14, 1996 filing dates which would antedate the Glenn document. The Office asserts the instant application is entitled only to the filing date of the provisional application, US Appl. No. 60/137,790, filed June 3, 1999.

However, contrary to the position of the Office, the Glenn document is not proper prior art. Applicants submit herewith a declaration under 37 CFR § 1.132 by Glenn [the Glenn declaration]. The Glenn declaration states co-authors Tanya Scharton-Kersten, Russell Vassell, and Gary R Matyas did not contribute to the conception of the invention as disclosed and claimed in the instant application and worked under the supervision and control of Dr. Glenn. The Glenn document, published in March 1999, was published within one year of the claimed priority date (June 3, 1999) and does not disclose an invention "by another." In view of the declaration, stating only inventors Glenn and Alving contributed to the conception of the invention as disclosed in the Glenn publication, it is believed the rejection is now moot. The Glenn document does not anticipate claims 1, 4, 13 and new claims 26-28. Reconsideration and withdrawal of the rejection is respectfully requested.

Rejection of claims 1-17 under 35 U.S.C. § 102(e)

The rejection of claims 1-17 under 35 U.S.C. § 102(e) as being anticipated by USPN 5,980,898 by Glenn *et al.* ['898] has been maintained. The rejection is respectfully traversed. Claims 2, 3, 6, 9, 10, 12 and 17 have been cancelled.

The Office alleges that the '898 patent (filed July 17, 1997) teaches the transcutaneous immunization system as claimed in claims 1-17. However, contrary to the position of the Office,

the '898 patent does not anticipate or render obvious the invention of claims 1, 4, 5, 7, 8, 11, 13-16 and new claims 26-28.

The '898 patent does not teach each and every element of currently amended claim 1, or, previous claim 1. The Office very clearly points out (Office Action, page 3, third full paragraph) that

> "the recitation of 'a marking formulation; said marking formulation comprising at least one chemical indicator, the presence of said indicator serving to provide a readily discernible indication of the use of said immunization formulation' in base claim has **no support** in USSN 08/896,085, filed July 1997, now US Pat No. 5,980,898, which in turn is a continuation-in-part of Serial No. 08/749,164, filed Nov. 14, 1996, now US Pat No. 5,910,306." [emphasis added]

Since the phrase "said marking formulation comprising at least one chemical indicator, the presence of said chemical indicator serving to provide a readily discernible indication of the use of said immunization formulation" occurs in newly amended claim 1, and the Office asserts the '898 patent does not have support for that phrase, the '898 patent does not teach each and every element of the claim. Since the '898 patent does not teach each and every element of the claim, the '898 patent cannot anticipate the invention as claimed. Further, since the dependent claims include all the limitations of the independent claim from which they depend, dependent claims 4, 5, 7, 8, 11, 13-16 and new claims 26-28 are not anticipated by the '898 patent.

In addition, since the '898 patent is silent on the concept of the element of "an indicator serving to provide a readily discernible indication of the use of the formulation," the '898 patent cannot provide any suggestion or motivation to one of ordinary skill to modify the invention claimed therein so as to arrive at the claimed invention. Therefore, the '898 patent does not render obvious the invention of claim 1 or claims 4, 5, 7, 8, 11, 13-16 and new claims 26-28 dependent therefrom.

The denial of the earliest claimed priority date back to the '898 patent, due to an alleged lack of support for the phrase "an indicator serving to provide a readily discernible indication of the use of the formulation," is an admission by the Office that the '898 patent does not teach or suggest each and every element of claim 1. In view of the arguments above and amendments to the claims, the rejection is believed to be overcome. Reconsideration and withdrawal of the rejection is respectfully requested.

Rejection of claims 1 and 14-20 under 35 U.S.C. § 103(a)

Claims 1 and 14-20 remain rejected under 35 U.S.C. § 103(a) as being unpatentable over USPN 5,980,898 (Glenn *et al.*) ['898] in view of USPN 4,834,985 (Larson *et al.*) [Larson]; USPN 6,180,136 (Elger *et al.*)[Elger] and Iizuka (Agents Actions 11(3): 254-9, 1981) [Iizuka]. The rejection is respectfully traversed. Claims 17, 19 and 20 have been cancelled.

The Office alleges claims 1 and 14-20 are rendered obvious by the '898 patent in view of the Larson, Elger and Iizuka documents. The Office cites the '898 patent for the teachings as discussed above. Elger is cited for teaching the use of cyclodextrins for the controlled release of pharmaceutically active compounds. Larson is cited for teaching the formulation of a phospholipid coated microcrystals for sustained release of pharmacologically active compounds to be delivered by means of air guns. Iizuka is cited for teaching applying a formulation to the inside surface of the ear or dorsal area as opposed to licking by applying the formulation to the frontal area. The Office asserts it would have been obvious to one of ordinary skill at the time the invention was made to produce a control and/or sustained release transcutaneous immunization system as taught by the '898 patent by substituting the formulation of the matrix or reservoir as taught by Elger or Larson to be delivered by means of an air gun as taught by Elger or formulated to inhibit the animal from licking the formulation as taught by Iizuka for the same purpose of immunizing a subject using a need as taught by the '898 patent, Elger, Larson and Iizuka.

However, the '898 patent does not teach each and every element of the claim 1 as set forth above and those arguments are incorporated herein. None of Larson, Elger, or Iizuka, taken alone or together, suggest "an indicator serving to provide a readily discernible indication of the use of the formulation" comprising an antigen and an adjuvant which induces an antigen specific immune response, and thus cure the deficiency of the '898 patent. Therefore, independent claim 1 is not obvious over the cited documents. Further, since dependent claims include all the limitations of the independent claim from which they depend, dependent claims 14-16 and 18 are not obvious over the '898 patent, Larson, Elger or Iizuka, taken alone or together. Thus, claims 1, 14-16, 18 and new claims 26-28 are free of the prior art.

The rejection is believed to be moot in view of the amendments to the claims and the arguments above. Reconsideration and withdrawal of the rejection is respectfully requested.

New grounds of rejection

Rejection under 35 U.S.C. § 112, second paragraph

Claims 6, 10, 11, 13, 15 and 16 have been rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. The rejection is respectfully traversed. Claims 6 and 10 have been cancelled.

The Office asserts the recitation of "said antigen" in claim 6 lacks antecedent basis in base claim 4. Claim 6 has been cancelled and therefore the rejection is moot.

The Office asserts the recitation of "indicator" in claim 10 has no antecedent basis in claim 2. Claim 10 has been cancelled, thus mooting the rejection.

The Office asserts the recitation of "paint" and "powders" in claim 13 is ambiguous and indefinite because one of ordinary skill cannot appraise the metes and bounds of the claimed invention. The Office also argues that some paints are toxic and not appropriate for *in vivo* use.

Without acquiescing to the position of the Office, claim 13 has been amended to delete "paint" and "powders." The fact that some paints may be toxic is irrelevant to the issue at hand.

The Office asserts the recitation of "said applicator" in claim 15 has no antecedent basis in claim 10. The Office suggests amending claim 10 to depend from claim 14. However, claim 10 has been cancelled. Claim 15 has been amended to depend from claim 14, which has support for "said applicator."

In view of the amendments to the claims, reconsideration and withdrawal of the rejection is respectfully requested.

Rejection of claims 1-7, 10-13 and 17 under 35 U.S.C. § 102(b)

Claims 1-7, 10-13 and 17 have been rejected under 35 U.S.C. § 102(b) as being anticipated by USPN 4,152,412 (Brewer) ['412]. The rejection is respectfully traversed. Claims 2, 3, 6, 10, 12 and 17 have been cancelled.

The Office asserts the '412 patent teaches an immunization formulation comprising at least one antigen, and a number of chemical indicators which serve to provide a readily discernible indication of the use of the immunization formulation. The Office notes the reference antigen (*Brucella abortus* specific antigen) inherently induces the *Brucella abortus* specific antigen specific immune response in the subject. The Office discusses other teachings in the '412 patent allegedly anticipating the invention and sums up the teachings of the '412 patent saying "a composition is a composition irrespective of its intended use."

However, independent claim 1 has been amended to now recite methods, not a composition. In addition, claim 1, part b) requires the adjuvant to induce the antigen specific immune response, not the antigen. Further, the '412 patent discloses administration of a formulation by injection, not application to the skin as is claimed in claim 1. Therefore, the '412 document fails to teach each and every element of claim 1.

As discussed above, since the '412 document fails to teach each and every element of the claim, the document cannot anticipate the invention. Reconsideration and withdrawal of the rejection is respectfully requested.

Rejection of claims 1, 8, 9 and 14-16 under 35 U.S.C. § 103(a)

Claims 1, 8, 9 and 14-16 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over USPN 4,152,412 (Brewer)['412] in view of USPN 5,667,798(Royds *et al.*)['798]. The rejection is respectfully traversed. Claim 9 has been cancelled.

The Office applies the teachings of the '412 patent as discussed above. The Office further distinguishes the difference between the invention of claims 9, 14, 15, and 16 and the '412 patent. The Office argues the '798 patent teaches an applicator such as a transdermal patch comprising a formulation such as drugs, local anesthesia and multicolor indicators that are designed to change with time, the dose delivered or to change color when the drug reserves have been depleted.

However, contrary to the position of the Office, neither the '412 patent or the '798 patent, taken alone or together, render obvious claims 1, 8 and 14-16. The '412 patent, teaching injection of a composition comprising a vaccine, has been previously discussed and those arguments are incorporated herein. The '412 patent is silent on **application** of the vaccine **to skin** and inducing an immune response to an antigen. The '798 patent discloses administration of therapeutic agents, not antigens and adjuvants, to the skin using the patch. The '798 patent is silent on the application of a formulation comprising at least one antigen and at least on adjuvant to the skin and does not provide any suggestion or motivation to modify the administered pharmaceutical composition with a solution inducing an antigen specific immune response. Neither the '412 patent nor the '798 patent provide the suggestion or motivation to modify the teachings of one with the teachings of the other so as to arrive at a method for inducing an antigen specific immune response, wherein the presence of the indicator is a readily discernible indication of

the use of the formulation as is claimed in claim 1. In view of the amendments to the claims and arguments herein, reconsideration and withdrawal of the rejection is respectfully requested.

Rejection of claims 18-20 under 35 U.S.C. § 103(a)

Claims 18-20 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over USPN 4,152,412 (Brewer) ['412] in view of USPN 5,667,798 (Royds) ['798] as applied to claims 1, 8, 9 and 14-16 above and further in view of USPN 6,180,136 (Larson) ['136] and Iizuka. The rejection is respectfully traversed. Claims 19 and 20 have been cancelled.

The Office asserts the teachings of the '898 and '798 patent as discussed above(the Office presumably is referring to the '412 patent and not the '898 patent). The Office cites the '136 patent to teach a formulation comprising phospholipid coated microcrystals for sustained release of pharmacologically active compounds to be delivered by means of an air gun. Iizuka is cited to teach a method for inhibiting animals from licking the formulation by applying the formulation to the inside surface of the ear or to the dorsal area.

However, contrary to the position of the Office, none of the documents taken alone or together render obvious the invention as claimed in claim 18. The arguments concerning the failure of the '412 and '798 patents to render obvious the invention as claimed in claims 1, 8 and 14-16 are set forth above and are incorporated herein. Briefly, the '412 patent, teaches injection of a composition comprising a vaccine. The '412 patent is silent on application of the vaccine **to skin** and inducing an immune response to an antigen. The '798 patent discloses administration of therapeutic agents to the skin using the patch. The '798 patent is silent on the application of a formulation comprising at least one antigen and at least on adjuvant to the skin and does not provide any suggestion or motivation to substitute the administered pharmaceutical composition with a solution inducing an antigen specific immune response. Neither the '412 patent nor the '798 patent provide the suggestion or motivation to modify the teachings of one with the teachings of the other so as to arrive at a "method for inducing an antigen specific immune response, wherein the presence of the indicator is a readily discernible indication of the use of

the formulation" as is presently claimed in claim 1.

The teachings of the '136 patent and Iizuka fail to cure the deficiency of the '412 and '798 patents. Since no document cited herein, taken alone or together, suggests the invention as claimed in claim 18, the claim is free of the cited prior art. Reconsideration and withdrawal of the rejection is respectfully requested.

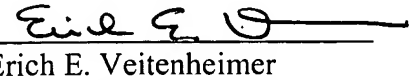
Conclusion

The foregoing amendments and remarks are being made to place the application in condition for allowance. Applicants respectfully request reconsideration and the timely allowance of the pending claims. A favorable action is awaited. Should the Examiner find that an interview would be helpful to further prosecution of this application, the Examiner is invited to telephone the undersigned at his convenience.

Except for issue fees payable under 37 C.F.R. § 1.18, the Commissioner is hereby authorized by this paper to charge any additional fees during the entire pendency of this application including fees due under 37 C.F.R. § 1.16 and § 1.17 which may be required, including any required extension of time fees, or credit any overpayment to Deposit Account No. 50-0310. This paragraph is intended to be a **constructive petition for extension of time** in accordance with 37 C.F.R. § 1.136(a)(3).

Attachment: Declaration under 37 CFR § 1.132 by Dr. Glenn

Respectfully submitted,
Morgan, Lewis & Bockius LLP



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PATENT
Atty. Dkt. No. : 056707-5005-01 US

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Glenn *et al.*	)	Group Art Unit: 1644
Application No.: **10/658,418**	)	Examiner: **Huynh, Phuong N.**
Filed: September 10, 2003	)	
Title: Indicators for Monitoring the Technique of Transcutaneous Immunization	)	

Commissioner for Patents
Washington, D.C.

Sir:

DECLARATION UNDER 37 C.F.R. § 1.132

I, Gregory M. Glenn, do hereby make the following declaration:

1. I am an inventor listed on Application No. 10/658,418, and I am an author of the scientific paper "Transcutaneous Immunization with Bacterial ADP-Ribosylating Exotoxins as Antigens and Adjuvants," *Infection and Immunity* 67(3): 1100-1106, published March, 1999.

2. I am familiar with the subject matter contributed by each individual listed as an author of the above referenced *Infection and Immunity* article.

3. Tanya Scharton-Kersten, a co-author of the above referenced paper, was a research associate working under my direction and control.

4. Russell Vassell, a co-author of the above referenced paper, was a research associate working under my direction and control.

5. Gary R. Matyas, a co-author of the above referenced paper, was a research associate working under my direction and control.

6. The authors, other than Dr. Carl Alving and myself, listed on the referenced *Infection and Immunity* journal article, did not contribute to the conception of the invention disclosed and claimed in the instant application.

I further declare that all statements made herein of my own knowledge are true, and that all statements made on information and belief are believed to be true, and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

By: _____
Gregory M. Glenn, M.D.

Dated: _____